P&T OFFICE ACKNOWLEDGEMENT

ATTORNEY	DATE
Sheldon O. Heber	01/24/07

CASE NUMBER/	SERIAL NUMBER
21564YP	10/577,893

DATE FILED
May 1, 2006

APPLICANT
Ludmerer, Steven W. et al.

EXPRESS MAIL NO.

The Patent & Trademark Office acknowledges, and has stamped hereon, the date of the receipt of the items checked below:

- ☒ AMENDMENT
- ☐ APPEAL AND FEE
- ☐ ASSIGNMENT
- ☐ BRIEF
- ☐ CERTIFICATE OF CORRECTION
- ☐ FINAL FEE
- ☐ LETTER
- ☐ REQUEST FOR F.F. LICENSE
- ☐ INFORMATION DISCLOSURE STATEMENT
- ☐ PTO 1449 & REFERENCES
- ☐ PETITION FOR EXTENSION OF TIME & FEE
- ☐ INVITATION TO CORRECT
- ☐ DEMAND-CHAPTER II & FEE SHEET
- x Sequence Listing w/Disk
- x Notice to Comply. . . Seq Discl.
- x Raw Sequence Listing Error Report

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Ludmerer, Steven W. *et al.*	Art Unit:
Serial No.:	10/577,893 Case No.: 21564YP	
Filed:	May 1, 2006	Examiner:
For:	HCV REPLICONS CONTAINING NS5B FROM GENOTYPE 2B	

Commission for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DOCKETED

JAN 2 4 2007

LOEB SCHAFFER

AMENDMENT

Sir:

Responsive to the Notice to Comply mailed January 5, 2007, applicants request the present application be amended as follows:

Amendments to the Specification begin on page 2 of this paper.

Remarks/Arguments begin on page 3 of this paper.

Amendments to the Specification:

Please amend the specification by entering the enclosed Sequence Listing.

Remarks/Arguments

Enclosed with the present amendment is a copy of the Notice to Comply, the sequence listing printout accompanying the Notice to Comply, and an amended Sequence Listing provided in hard copy and computer readable form. The amendments to the Sequence Listing update the general information section and correct the description of features indicated in the Notice to Comply for SEQ ID NOs: 1, 24 and 27. The description for SEQ ID NO: 1 was amended to indicate Xaa in position 392, instead of position 376. The description for SEQ ID NO: 24 was amended to provide a correct spelling for "Artificial". The description for SEQ ID NO: 27 was amended to indicate "Artificial".

No new matter is introduced into the Sequence Listing. I hereby state that the contents of the paper and computer readable copies of the enclosed Sequence Listing are the same.

Please charge deposit account 13-2755 for fees due in connection with this amendment. If any time extensions are needed for the timely filing of the present amendment, applicants petition for such extensions and authorize the charging of deposit account 13-2755 for the appropriate fees.

Respectfully submitted,

By _Sheldon Heber_
Sheldon O. Heber
Reg. No. 38,179
Attorney for Applicant(s)

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SEQUENCE LISTING

<110> Ludmerer, Steven W.
      Graham, Donald J.
      LaFemina, Robert L.
      Flores, Osvaldo A.
      Pizzuti, Maura
      Traboni, Cinzia

<120> HCV REPLICONS CONTAINING NS5B FROM
   GENOTYPE 2B

<130> 21564YP

<140> 10/577,893
<141> 2006-05-01

<150> PCT/US2004/036575
<151> 2004-11-03

<150> 60/517,605
<151> 2003-11-05

<160> 28

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 591
<212> PRT
<213> Artificial Sequence

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<223> Xaa = threonine or serine

<221> VARIANT
<222> (24)...(24)
<223> Xaa = asparagine or serine

<221> VARIANT
<222> (31)...(31)
<223> Xaa = methionine or isoleucine

<221> VARIANT
<222> (392)...(392)
<223> Xaa = isoleucine or leucine

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1   5   10   15

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Phe His Asn Lys Val Tyr Ser Thr Thr Ser Arg Ser Ala Ser Leu Arg
        35                  40                  45
Ala Lys Lys Val Thr Phe Asp Arg Val Gln Val Leu Asp Ala His Tyr
    50                  55                  60
Asp Ser Val Leu Gln Asp Val Lys Arg Ala Ala Ser Lys Val Ser Ala
65                  70                  75                      80
Arg Leu Leu Thr Val Glu Glu Ala Cys Ala Leu Thr Pro Pro His Ser
             85                  90                  95
Ala Lys Ser Arg Tyr Gly Phe Gly Ala Lys Glu Val Arg Ser Leu Ser
            100                 105                 110
Arg Arg Ala Val Asn His Ile Arg Ser Val Trp Glu Asp Leu Leu Glu
        115                 120                 125
Asp Gln His Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val
    130                 135                 140
Phe Cys Ile Asp Pro Thr Lys Gly Gly Lys Lys Pro Ala Arg Leu Ile
145                 150                 155                     160
Val Tyr Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr
             165                 170                 175
Asp Ile Ala Gln Lys Leu Pro Lys Ala Ile Met Gly Pro Ser Tyr Gly
            180                 185                 190
Phe Gln Tyr Ser Pro Ala Glu Arg Val Asp Phe Leu Leu Lys Ala Trp
            195                 200                 205
Gly Ser Lys Lys Asp Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe
    210                 215                 220
Asp Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile Tyr
225                 230                 235                     240
Gln Ala Cys Ser Leu Pro Gln Glu Ala Arg Thr Val Ile His Ser Leu
             245                 250                 255
Thr Glu Arg Leu Tyr Val Gly Gly Pro Met Thr Asn Ser Lys Gly Gln
            260                 265                 270
Ser Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser
            275                 280                 285
Met Gly Asn Thr Met Thr Cys Tyr Ile Lys Ala Leu Ala Ala Cys Lys
    290                 295                 300
Ala Ala Gly Ile Val Asp Pro Val Met Leu Val Cys Gly Asp Asp Leu
305                 310                 315                     320
Val Val Ile Ser Glu Ser Gln Gly Asn Glu Glu Asp Glu Arg Asn Leu
             325                 330                 335
Arg Ala Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp
            340                 345                 350
Leu Pro Arg Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser
        355                 360                 365
Asn Val Ser Val Ala Leu Asp Ser Arg Gly Arg Arg Arg Tyr Phe Leu
    370                 375                 380
Thr Arg Asp Pro Thr Thr Pro Xaa Thr Arg Ala Ala Trp Glu Thr Val
385                 390                 395                     400
Arg His Ser Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Gln Tyr Ala
             405                 410                 415
Pro Thr Ile Trp Val Arg Met Val Ile Met Thr His Phe Phe Ser Ile
            420                 425                 430
Leu Leu Ala Gln Asp Thr Leu Asn Gln Asn Leu Asn Phe Glu Met Tyr
        435                 440                 445
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Gly Ala Val Tyr Ser Val Asn Pro Leu Asp Leu Pro Ala Ile Ile Glu
    450                 455                 460
Arg Leu His Gly Leu Glu Ala Phe Ser Leu His Thr Tyr Ser Pro His
465                 470                 475                 480
Glu Leu Ser Arg Val Ala Ala Thr Leu Arg Lys Leu Gly Ala Pro Pro
                485                 490                 495
Leu Arg Ala Trp Lys Ser Arg Ala Arg Ala Val Arg Ala Ser Leu Ile
                500                 505                 510
Ala Gln Gly Ala Arg Ala Ala Ile Cys Gly Arg Tyr Leu Phe Asn Trp
            515                 520                 525
Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Leu Pro Glu Ala Ser Arg
    530                 535                 540
Leu Asp Leu Ser Gly Trp Phe Thr Val Gly Ala Gly Gly Gly Asp Ile
545                 550                 555                 560
Tyr His Ser Val Ser His Ala Arg Pro Arg Leu Leu Leu Leu Cys Leu
                565                 570                 575
Leu Leu Leu Ser Val Gly Val Gly Ile Phe Leu Leu Pro Asp Arg
            580                 585                 590
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<212> DNA
<213> Artificial Sequence

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<223> modified NS5B

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<223> n = A or T

<221> variation
<222> (9)...(9)
<223> n = C or A

<221> variation
<222> (13)...(13)
<223> n = A or T

<221> variation
<222> (15)...(15)
<223> n = A or C

<221> variation
<222> (21)...(21)
<223> n - A or G

<221> variation
<222> (24)...(24)
<223> n = C or G

<221> variation
<222> (28)...(28)
<223> n = T  or C
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<223> n = G or C

<221> variation
<222> (33)...(33)
<223> n = C or A

<221> variation
<222> (71)...(71)
<223> n = A or G

<221> variation
<222> (83)...(83)
<223> n = G or T

<221> variation
<222> (1174)...(1174)
<223> n = A or C

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acctcgagga gtgcctctct gagggcaaag aaggtgactt ttgacagggt gcaggtgctg 180
gacgcacact atgactcagt cttgcaggac gttaagcggg ccgcctctaa ggttagtgcg 240
aggctcctca cggtagagga agcctgcgcg ctgaccccgc cccactccgc caaatcgcga 300
tacggatttg gggcaaaaga ggtgcgcagc ttatctagga gggccgttaa ccacatccgg 360
tccgtgtggg aggacctcct ggaagaccaa cataccccaa ttgacacaac tatcatggct 420
aaaaatgagg tgttctgcat tgatccaact aaaggtggga aaaagccagc tcgcctcatc 480
gtataccccg accttggggt cagggtgtgc gaaaagatgg ccctctatga catcgcacaa 540
aagcttccca aagcgataat ggggccatcc tatgggttcc aatactctcc cgcagaacgg 600
gtcgatttcc tcctcaaagc ttggggaagt aagaaggacc caatggggtt ctcgtatgac 660
acccgctgct ttgactcaac cgtcacggag agggacataa gaacagaaga atccatatat 720
caggcttgtt ctctgcctca agaagccaga actgtcatac actcgctcac tgagagactt 780
tacgtaggag ggcccatgac aaacagcaaa gggcaatcct gcggctacag gcgttgccgc 840
gcaagcggtg ttttcaccac cagcatgggg aataccatga catgttacat caaagccctt 900
gcagcgtgta aggctgcagg gatcgtggac cctgttatgt tggtgtgtgg agacgacctg 960
gtcgtcatct cagagagcca aggtaacgag gaggacgagc gaaacctgag agctttcacg 1020
gaggctatga ccaggtattc cgcccctccc ggtgaccttc ccagaccgga atatgacttg 1080
gagcttataa catcctgctc ctcaaacgta tcggtagcgc tggactctcg gggtcgccgc 1140
cggtacttcc taaccagaga ccctaccact ccantcaccc gagctgcttg ggaaacagta 1200
agacactccc ctgtcaattc ttggctgggc aacatcatcc agtacgcccc cacaatctgg 1260
gtccggatgg tcataatgac tcacttcttc tccatactat tggcccagga cactctgaac 1320
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gccataattg aaaggctaca tgggcttgaa gccttttcac tgcacacata ctctccccac 1440
gaactctcac gggtggcagc aactctcaga aaacttggag cgcctcccct tagagcgtgg 1500
aagagtcggg cgcgtgccgt gagagcttca ctcatcgccc aaggagcgag ggcggccatt 1560
tgtggccgct acctcttcaa ctgggcggtg aaaacaaagc tcaaactcac tccattgccc 1620
gaggcgagcc gcctggattt atccgggtgg ttcaccgtgg gcgccggcgg gggcgacatt 1680
tatcacagcg tgtcgcatgc ccgaccccgc ctattactcc tttgcctact cctacttagc 1740
gtaggagtag gcatcttttt actccccgat cgatga 1776

<210> 3
<211> 1394
<212> PRT
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<223> modified NS3-5A

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<223> Xaa = asparagine or serine

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<223> Xaa = valine or alanine

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Cys Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly
            20                  25                  30
Glu Val Gln Val Val Ser Thr Ala Thr Gln Ser Phe Leu Ala Thr Cys
            35                  40                  45
Val Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Ser Lys Thr
    50                  55                  60
Leu Ala Gly Pro Lys Gly Pro Ile Thr Gln Met Tyr Thr Asn Val Asp
65                  70                  75                  80
Gln Asp Leu Val Gly Trp Gln Ala Pro Pro Gly Ala Arg Ser Leu Thr
            85                  90                  95
Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala
            100                 105                 110
Asp Val Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu
            115                 120                 125
Ser Pro Arg Pro Val Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu
    130                 135                 140
Leu Cys Pro Ser Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys
145                 150                 155                 160
Thr Arg Gly Val Ala Lys Ala Val Asp Phe Val Pro Val Glu Ser Met
            165                 170                 175
Glu Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro
            180                 185                 190
Ala Val Pro Gln Thr Phe Gln Val Ala His Leu His Ala Pro Thr Gly
    195                 200                 205
Ser Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr
    210                 215                 220
Lys Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly
225                 230                 235                 240
Ala Tyr Met Ser Lys Ala His Gly Ile Asp Pro Asn Ile Arg Thr Gly
            245                 250                 255
Val Arg Thr Ile Thr Thr Gly Ala Pro Val Thr Tyr Ser Thr Tyr Gly
            260                 265                 270
Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile
    275                 280                 285
Ile Cys Asp Glu Cys His Ser Thr Asp Ser Thr Thr Ile Leu Gly Ile
    290                 295                 300
Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val
305                 310                 315                 320
```

```
Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn
            325             330             335
Ile Glu Glu Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr Gly
            340             345             350
Lys Ala Ile Pro Ile Glu Ala Ile Arg Gly Gly Arg His Leu Ile Phe
            355             360             365
Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Ser Gly
        370             375             380
Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val
385             390             395             400
Ile Pro Thr Ile Gly Asp Val Val Val Ala Thr Asp Ala Leu Met
            405             410             415
Thr Gly Tyr Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys
            420             425             430
Val Thr Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu
            435             440             445
Thr Thr Thr Val Pro Gln Asp Ala Val Ser Arg Ser Gln Arg Arg Gly
    450             455             460
Arg Thr Gly Arg Gly Arg Met Gly Ile Tyr Arg Phe Val Thr Pro Gly
465             470             475             480
Glu Arg Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr
            485             490             495
Asp Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Ser Val
            500             505             510
Arg Leu Arg Ala Tyr Leu Asn Thr Pro Gly Leu Pro Val Cys Gln Asp
        515             520             525
His Leu Glu Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile Asp
    530             535             540
Ala His Phe Leu Ser Gln Thr Lys Gln Ala Gly Asp Asn Phe Pro Tyr
545             550             555             560
Leu Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro
            565             570             575
Pro Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr
            580             585             590
Leu His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn
    595             600             605
Glu Val Thr Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met
    610             615             620
Ser Ala Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly Gly
625             630             635             640
Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Thr Thr Gly Ser Val Val
            645             650             655
Ile Val Gly Arg Ile Ile Leu Ser Gly Arg Pro Ala Ile Val Pro Asp
            660             665             670
Arg Glu Phe Leu Tyr Gln Glu Phe Asp Glu Met Glu Glu Cys Ala Ser
        675             680             685
His Leu Pro Tyr Ile Glu Gln Gly Met Gln Leu Ala Glu Gln Phe Lys
    690             695             700
Gln Lys Ala Leu Gly Leu Leu Gln Thr Ala Thr Lys Gln Ala Glu Ala
705             710             715             720
Ala Ala Pro Val Val Glu Ser Lys Trp Arg Ala Leu Glu Thr Phe Trp
            725             730             735
Ala Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly
            740             745             750
```

-6-

```
Leu Ser Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe
    755                 760                 765
Thr Ala Ser Ile Thr Ser Pro Leu Thr Thr Gln Ser Thr Leu Leu Phe
    770                 775                 780
Asn Ile Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Pro Pro Ser Ala
785                 790                 795                 800
Ala Ser Ala Phe Val Gly Ala Gly Ile Ala Gly Ala Ala Val Gly Ser
                805                 810                 815
Ile Gly Leu Gly Lys Val Leu Val Asp Ile Leu Ala Gly Tyr Gly Ala
                820                 825                 830
Gly Val Ala Gly Ala Leu Val Ala Phe Lys Val Met Ser Gly Glu Met
    .835                840                 845
Pro Ser Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro
    850                 855                 860
Gly Ala Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His
865                 870                 875                 880
Val Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala
                885                 890                 895
Phe Ala Ser Arg Gly Asn His Xaa Ser Pro Thr His Tyr Val Pro Glu
    900                 905                 910
Ser Asp Ala Ala Ala Arg Val Thr Gln Ile Leu Ser Ser Leu Thr Ile
    915                 920                 925
Thr Gln Leu Leu Lys Arg Leu His Gln Trp Ile Asn Glu Asp Cys Ser
    930                 935                 940
Thr Pro Cys Ser Gly Ser Trp Leu Arg Asp Val Trp Asp Trp Ile Cys
945                 950                 955                 960
Thr Val Leu Thr Asp Phe Lys Thr Trp Leu Gln Ser Lys Leu Leu Pro
                965                 970                 975
Gln Leu Pro Gly Val Pro Phe Phe Ser Cys Gln Arg Gly Tyr Lys Gly
                980                 985                 990
Val Trp Arg Gly Asp Gly Ile Met Gln Thr Thr Cys Pro Cys Gly Ala
    995                 1000                1005
Gln Ile Thr Gly His Val Lys Asn Gly Ser Met Arg Ile Val Gly Pro
    1010                1015                1020
Lys Thr Cys Ser Asn Thr Trp His Gly Thr Phe Pro Ile Asn Ala Tyr
1025                1030                1035                1040
Thr Thr Gly Pro Cys Thr Pro Ser Pro Ala Pro Asn Tyr Ser Arg Ala
                1045                1050                1055
Leu Trp Arg Val Ala Ala Glu Glu Tyr Val Glu Val Thr Arg Val Gly
                1060                1065                1070
Asp Phe His Tyr Val Thr Gly Met Thr Thr Asp Asn Val Lys Cys Pro
    1075                1080                1085
Cys Gln Val Pro Ala Pro Glu Phe Phe Thr Glu Val Asp Gly Val Arg
    1090                1095                1100
Leu His Arg Tyr Ala Pro Ala Cys Arg Pro Leu Leu Arg Glu Glu Val
1105                1110                1115                1120
Thr Phe Gln Val Gly Leu Asn Gln Tyr Leu Val Gly Ser Gln Leu Pro
                1125                1130                1135
Cys Glu Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp
                1140                1145                1150
Pro Ser His Ile Thr Ala Glu Thr Ala Lys Arg Arg Leu Ala Arg Gly
    1155                1160                1165
Ser Pro Pro Ser Leu Ala Ser Ser Ser Ala Ile Gln Leu Ser Ala Pro
    1170                1175                1180
```

```
Ser Leu Lys Ala Thr Cys Thr Thr His His Val Ser Pro Asp Ala Asp
1185                1190                1195                1200
Leu Ile Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Xaa Ile
                1205                1210                1215
Thr Arg Val Glu Ser Glu Asn Lys Val Val Val Leu Asp Ser Phe Asp
                1220                1225                1230
Pro Leu Arg Ala Glu Glu Asp Glu Arg Glu Val Ser Val Pro Ala Glu
                1235                1240                1245
Ile Leu Arg Lys Ser Lys Lys Phe Pro Ala Ala Met Pro Ile Trp Ala
                1250                1255                1260
Arg Pro Asp Tyr Asn Pro Pro Leu Leu Glu Ser Trp Lys Asp Pro Asp
1265                1270                1275                1280
Tyr Val Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Ile Lys Ala
                1285                1290                1295
Pro Pro Ile Pro Pro Pro Arg Arg Lys Arg Thr Val Val Leu Thr Glu
                1300                1305                1310
Ser Ser Val Ser Ser Ala Leu Ala Glu Leu Ala Thr Lys Thr Phe Gly
                1315                1320                1325
Ser Ser Glu Ser Ser Ala Val Asp Ser Gly Thr Ala Thr Ala Leu Pro
                1330                1335                1340
Asp Gln Ala Ser Asp Asp Gly Asp Lys Gly Ser Asp Val Glu Ser Tyr
1345                1350                1355                1360
Ser Ser Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser
                1365                1370                1375
Asp Gly Ser Trp Ser Thr Val Ser Glu Glu Ala Ser Glu Asp Val Val
                1380                1385                1390
Cys Cys
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<210> 4
<211> 4182
<212> DNA
<213> Artificial Sequence

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<223> modified NS3-5A

<221> variation
<222> (2711)...(2711)
<223> n = T or C

<221> variation
<222> (3645)...(3645)
<223> n = A or G

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acacaatcct tcctggcgac ctgcgtcaac ggcgtgtgtt ggaccgttta ccatggtgct 180
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acccgggggg ttgcgaaggc ggtggacttt gtgcccgtag agtccatgga aactactatg 540
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```
cggtctccgg  tcttcacgga  caactcatcc  ccccggccg   taccgcagac  atttcaagtg  600
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gccctgtcta  atactggaga  gatccccttc  tatggcaaag  ccatccccat  tgaagccatc  1080
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ggcgactttg  actcagtgat  cgactgtaac  acatgtgtca  cccagacagt  cgacttcagc  1320
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gcttggtacg  agctcacccc  cgccgagacc  tcggttaggt  tgcgggccta  cctgaacaca  1560
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tacaggctgg  gagccgtcca  aaatgaggtc  accctcaccc  accccataac  caaatacatc  1860
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-9-

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Gln Asp Ile Gln Pro Ala Ile Gln Ser Ser Trp Pro Lys Leu Glu Gln
           35                  40                  45
Phe Trp Ala Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu
       50                  55                  60
Ala Gly Leu Ser Thr Leu Pro Gly Asn Pro Ala Val Ala Ser Met Met
65                  70                  75                  80
Ala Phe Ser Ala Ala Leu Thr Ser Pro Leu Pro Thr Ser Thr Thr Ile
               85                  90                  95
Leu Leu Asn Ile Met Gly Gly Trp Leu Ala Ser Gln Ile Ala Pro Pro
               100                 105                 110
Ala Gly Ala Thr Gly Phe Val Val Ser Gly Leu Val Gly Ala Ala Val
           115                 120                 125
Gly Ser Ile Gly Leu Gly Lys Ile Leu Val Asp Val Leu Ala Gly Tyr
       130                 135                 140
Gly Ala Gly Ile Ser Gly Ala Leu Val Ala Phe Lys Ile Met Ser Gly
145                 150                 155                 160
Glu Lys Pro Thr Val Glu Asp Val Val Asn Leu Leu Pro Ala Ile Leu
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Ser Pro Gly Ala Leu Val Val Gly Val Ile Cys Ala Ala Ile Leu Arg
           180                 185                 190
Arg His Val Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu
       195                 200                 205
Ile Ala Phe Ala Ser Arg Gly Asn His Ala Ser Pro Thr His Tyr Val
   210                 215                 220
Pro Glu Ser Asp Ala Ala Ala Arg Val Thr Gln Ile Leu Ser Ser Leu
225                 230                 235                 240
Thr Ile Thr Gln Leu Leu Lys Arg Leu His Gln Trp Ile Asn Glu Asp
               245                 250                 255
Cys Ser Thr Pro Cys
           260
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If you are not using EFS-Web to submit your reply, you must include a copy of this notice.

DEBORAH D WILLIAMS

Telephone: (703) 308-9140 EXT 205

PART 1 - ATTORNEY/APPLICANT COPY

U.S. APPLICATION NUMBER NO.	INTERNATIONAL APPLICATION NO.	ATTY. DOCKET NO.
10/577,893	PCT/US04/36575	21564Y

FORM PCT/DO/EO/922 (371 Formalities Notice)

STIC Biotechnology Systems Branch

RAW SEQUENCE LISTING
ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: _10/577, 893_

Source: _IFWP_

Date Processed by STIC: _05/11/2006_

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
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1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY
FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

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Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.
Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (**<http://www.uspto.gov/ebc/efs/downloads/documents.htm>** , **EFS Submission User Manual** - ePAVE)
2. **U.S. Postal Service:** Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
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Revised 01/10/06

IFWP

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

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        5        Istituto di Ricerche di Biologia Molecolare P. Angeletti S.p.A.
        7 <120> TITLE OF INVENTION: HCV REPLICONS CONTAINING NS5B FROM
        8        GENOTYPE 2B
       10 <130> FILE REFERENCE: 21564Y PCT
C--> 12 <140> CURRENT APPLICATION NUMBER: US/10/577,893
C--> 12 <141> CURRENT FILING DATE: 2006-05-01
       12 <150> PRIOR APPLICATION NUMBER: 60/517,605
       13 <151> PRIOR FILING DATE: 2003-11-05
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Does Not Comply
Corrected Diskette Needed
(pg 1, 2, 6, 7)

→ at this Location 'Ser'

→ at this location
392

Input Set : A:\21564Y SEQ 05 01 06.TXT
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 61     130                 135                 140
 62 Phe Cys Ile Asp Pro Thr Lys Gly Gly Lys Lys Pro Ala Arg Leu Ile
 63 145                 150                 155                 160
 64 Val Tyr Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr
 65                 165                 170                 175
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 67             180                 185                 190
 68 Phe Gln Tyr Ser Pro Ala Glu Arg Val Asp Phe Leu Leu Lys Ala Trp
 69     195                 200                 205
 70 Gly Ser Lys Lys Asp Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe
 71     210                 215                 220
 72 Asp Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile Tyr
 73 225                 230                 235                 240
 74 Gln Ala Cys Ser Leu Pro Gln Glu Ala Arg Thr Val Ile His Ser Leu
 75                 245                 250                 255
 76 Thr Glu Arg Leu Tyr Val Gly Gly Pro Met Thr Asn Ser Lys Gly Gln
 77     260                 265                 270
 78 Ser Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser
 79     275                 280                 285
 80 Met Gly Asn Thr Met Thr Cys Tyr Ile Lys Ala Leu Ala Ala Cys Lys
 81     290                 295                 300
 82 Ala Ala Gly Ile Val Asp Pro Val Met Leu Val Cys Gly Asp Asp Leu
 83 305                 310                 315                 320
 84 Val Val Ile Ser Glu Ser Gln Gly Asn Glu Glu Asp Glu Arg Asn Leu
 85                 325                 330                 335
 86 Arg Ala Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp
 87     340                 345                 350
 88 Leu Pro Arg Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser
 89     355                 360                 365
 90 Asn Val Ser Val Ala Leu Asp Ser Arg Gly Arg Arg Arg Tyr Phe Leu
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 93 385                 390                 395                 400
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 96 Pro Thr Ile Trp Val Arg Met Val Ile Met Thr His Phe Phe Ser Ile
 97                 420                 425                 430
 98 Leu Leu Ala Gln Asp Thr Leu Asn Gln Asn Leu Asn Phe Glu Met Tyr
 99     435                 440                 445
100 Gly Ala Val Tyr Ser Val Asn Pro Leu Asp Leu Pro Ala Ile Ile Glu
101     450                 455                 460
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RAW SEQUENCE LISTING   DATE: 05/11/2006
PATENT APPLICATION: US/10/577,893   TIME: 11:07:16

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Output Set: N:\CRF4\05112006\J577893.raw


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     111         530                 535                 540
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     113 545                 550                 555                 560
     114 Tyr His Ser Val Ser His Ala Arg Pro Arg Leu Leu Leu Leu Cys Leu
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    202 aagagtcggg cgcgtgccgt gagagcttca ctcatcgccc aaggagcgag ggcggccatt 1560
    203 tgtggccgct acctcttcaa ctgggcggtg aaaacaaagc tcaaactcac tccattgccc 1620
    204 gaggcgagcc gcctggattt atccgggtgg ttcaccgtgg gcgccggcgg gggcgacatt 1680
    205 tatcacagcg tgtcgcatgc ccgaccccgc ctattactcc tttgcctact cctacttagc 1740
    206 gtaggagtag gcatcttttt actccccgat cgatga 1776
    208 <210> SEQ ID NO: 3
    209 <211> LENGTH: 1394
    210 <212> TYPE: PRT
    211 <213> ORGANISM: Artificial Sequence
    213 <220> FEATURE:
    214 <223> OTHER INFORMATION: modified NS3-5A
W--> 216 <221> NAME/KEY: VARIANT
    217 <222> LOCATION: (1215)...(1215)
    218 <223> OTHER INFORMATION: Xaa = asparagine or serine
W--> 220 <221> VARIANT
    221 <222> LOCATION: (904)...(904)
    222 <223> OTHER INFORMATION: Xaa = valine or alanine
W--> 224 <400> 3
```

RAW SEQUENCE LISTING   DATE: 05/11/2006
PATENT APPLICATION: US/10/577,893   TIME: 11:07:16

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

```
225 Met Ala Pro Ile Thr Ala Tyr Ser Gln Gln Thr Arg Gly Leu Leu Gly
226  1               5                   10                  15
227 Cys Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly
228             20                  25                  30
229 Glu Val Gln Val Val Ser Thr Ala Thr Gln Ser Phe Leu Ala Thr Cys
230         35                  40                  45
231 Val Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Ser Lys Thr
232     50                  55                  60
233 Leu Ala Gly Pro Lys Gly Pro Ile Thr Gln Met Tyr Thr Asn Val Asp
234 65                  70                  75                  80
235 Gln Asp Leu Val Gly Trp Gln Ala Pro Pro Gly Ala Arg Ser Leu Thr
236                 85                  90                  95
237 Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala
238             100                 105                 110
239 Asp Val Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu
240         115                 120                 125
241 Ser Pro Arg Pro Val Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu
242         130                 135                 140
243 Leu Cys Pro Ser Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys
244 145             150                 155                 160
245 Thr Arg Gly Val Ala Lys Ala Val Asp Phe Val Pro Val Glu Ser Met
246             165                 170                 175
247 Glu Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro
248             180                 185                 190
249 Ala Val Pro Gln Thr Phe Gln Val Ala His Leu His Ala Pro Thr Gly
250         195                 200                 205
251 Ser Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr
252         210                 215                 220
253 Lys Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly
254 225                 230                 235                 240
255 Ala Tyr Met Ser Lys Ala His Gly Ile Asp Pro Asn Ile Arg Thr Gly
256             245                 250                 255
257 Val Arg Thr Ile Thr Thr Gly Ala Pro Val Thr Tyr Ser Thr Tyr Gly
258             260                 265                 270
259 Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile
260         275                 280                 285
261 Ile Cys Asp Glu Cys His Ser Thr Asp Ser Thr Thr Ile Leu Gly Ile
262     290                 295                 300
263 Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val
264 305             310                 315                 320
265 Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn
266             325                 330                 335
267 Ile Glu Glu Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr Gly
268             340                 345                 350
269 Lys Ala Ile Pro Ile Glu Ala Ile Arg Gly Gly Arg His Leu Ile Phe
270         355                 360                 365
271 Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Ser Gly
272         370                 375                 380
273 Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val
```

```
<210> 24
<211> 19
<212> DNA
<213> Artifial Sequence
```
→

```
<400> 24
gtctaccgtg agcgaggaa
```

If <213> Responses are
Artificial or Unknown.
Pls Explain the Source
of genetic Material.
See Item 11 on Error
Summary Sheet.

```
<210> 27
<211> 783
<212> DNA
<213> modified NS4B
<400> 27
```

2137 Responses can only be Artificial, Unknown or Genus Species. See Item 10 on Error Summary Sheet.

RAW SEQUENCE LISTING ERROR SUMMARY   DATE: 05/11/2006
PATENT APPLICATION: US/10/577,893   TIME: 11:07:17

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

Please Note:
Use of n and/or Xaa have been detected in the Sequence Listing. Please review the
Sequence Listing to ensure that a corresponding explanation is presented in the <220>
to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:1; Xaa Pos. 5,24,31,392
Seq#:2; N Pos. 3,9,15,15,21,24,28,30,33,71,93,1174
Seq#:3; Xaa Pos. 904,1215
Seq#:4; N Pos. 3644

Use of <220> Feature(NEW RULES):
Sequence(s) are missing the <220> Feature and associated headings.
Use of <220> to <223> is MANDATORY if <213> ORGANISM is "Artificial Sequence"
or"Unknown". Please explain source of genetic material in <220> to <223>
section (See "Federal Register," 6/01/98, Vol. 63, No. 104,pp.29631-32)
(Sec.1.823 of new Rules)

Seq#:1,2,3,4,24

VERIFICATION SUMMARY   DATE: 05/11/2006
PATENT APPLICATION: US/10/577,893   TIME: 11:07:17

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

```
L:12 M:270 C: Current Application Number differs, Replaced Current Application No
L:12 M:271 C: Current Filing Date differs, Replaced Current Filing Date
L:27 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:31 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:35 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:39 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:43 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:44 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:0
L:46 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:16
L:92 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:384
L:128 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:132 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:136 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:140 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:144 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:148 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:152 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:156 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:160 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:164 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:168 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:172 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:176 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:177 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:0
L:178 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:60
L:196 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:1140
L:216 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:220 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:3
L:224 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:3
L:337 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:896
L:375 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:1200
L:411 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:415 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:4
L:419 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:4
L:480 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:4 after pos.:3600
L:703 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:24
L:705 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ#:24, <213>
ORGANISM:Artificial Sequence
L:705 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:24, <213>
ORGANISM:Artificial Sequence
L:705 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:24,Line#:705
```

STIC Biotechnology Systems Branch

RAW SEQUENCE LISTING
ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: _10/577, 893_
Source: _TFWP_
Date Processed by STIC: _05/11/2006_

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:
1) **INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,**
2) **TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY**
FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE **CHECKER VERSION 4.4.0 PROGRAM**, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:
http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.
Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.
Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (**<http://www.uspto.gov/ebc/efs/downloads/documents.htm>** , **EFS Submission User Manual** - ePAVE)
2. **U.S. Postal Service:** Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. **Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 01/14/05):** U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314

Revised 01/10/06

IFWP

```
RAW SEQUENCE LISTING                        DATE: 05/11/2006
PATENT APPLICATION:  US/10/577,893          TIME: 11:07:16

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

     4 <110> APPLICANT: Merck & Co., Inc.
     5         Istituto di Ricerche di Biologia Molecolare P. Angeletti S.p.A.
     7 <120> TITLE OF INVENTION: HCV REPLICONS CONTAINING NS5B FROM
     8         GENOTYPE 2B
    10 <130> FILE REFERENCE: 21564Y PCT
C--> 12 <140> CURRENT APPLICATION NUMBER: US/10/577,893
C--> 12 <141> CURRENT FILING DATE: 2006-05-01
    12 <150> PRIOR APPLICATION NUMBER: 60/517,605
    13 <151> PRIOR FILING DATE: 2003-11-05
    15 <160> NUMBER OF SEQ ID NOS: 28
    17 <170> SOFTWARE: FastSEQ for Windows Version 4.0
    19 <210> SEQ ID NO: 1
    20 <211> LENGTH: 591
    21 <212> TYPE: PRT
    22 <213> ORGANISM: Artificial Sequence
    24 <220> FEATURE:
    25 <223> OTHER INFORMATION: modified NS5B
W--> 27 <221> NAME/KEY: VARIANT
    28 <222> LOCATION: (5)...(5)
    29 <223> OTHER INFORMATION: Xaa = threonine or serine
W--> 31 <221> VARIANT
    32 <222> LOCATION: (24)...(24)
    33 <223> OTHER INFORMATION: Xaa = asparagine or serine
W--> 35 <221> VARIANT
    36 <222> LOCATION: (31)...(31)
    37 <223> OTHER INFORMATION: Xaa = methionine or isoleucine
W--> 39 <221> VARIANT
    40 <222> LOCATION: (376)...(376)
    41 <223> OTHER INFORMATION: Xaa = isoleucine or leucine
W--> 43 <400> 1
W--> 44 Ser Met Ser Tyr Xaa Trp Thr Gly Ala Leu Ile Thr Pro Cys Gly Pro
    45 1               5                  10                  15
W--> 46 Glu Glu Glu Lys Leu Pro Ile Xaa Pro Leu Ser Asn Ser Leu Xaa Arg
    47             20                  25                  30
    48 Phe His Asn Lys Val Tyr Ser Thr Thr Ser Arg Ser Ala Ser Leu Arg
    49             35                  40                  45
    50 Ala Lys Lys Val Thr Phe Asp Arg Val Gln Val Leu Asp Ala His Tyr
    51         50                  55                  60
    52 Asp Ser Val Leu Gln Asp Val Lys Arg Ala Ala Ser Lys Val Ser Ala
    53 65                  70                  75                  80
    54 Arg Leu Leu Thr Val Glu Glu Ala Cys Ala Leu Thr Pro Pro His Ser
    55                 85                  90                  95
    56 Ala Lys Ser Arg Tyr Gly Phe Gly Ala Lys Glu Val Arg Ser Leu Ser
```

Handwritten annotations: Does Not Comply / Corrected Diskette Needed (pg 1, 2, 6, 7) · at this location 'Ser' · at this location 'Ser' · at this location 392

RAW SEQUENCE LISTING   DATE: 05/11/2006
PATENT APPLICATION: US/10/577,893   TIME: 11:07:16

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

```
  57                    100                   105                   110
  58 Arg Arg Ala Val Asn His Ile Arg Ser Val Trp Glu Asp Leu Leu Glu
  59         115                   120                   125
  60 Asp Gln His Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val
  61     130                   135                   140
  62 Phe Cys Ile Asp Pro Thr Lys Gly Gly Lys Lys Pro Ala Arg Leu Ile
  63 145                   150                   155                   160
  64 Val Tyr Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr
  65                   165                   170                   175
  66 Asp Ile Ala Gln Lys Leu Pro Lys Ala Ile Met Gly Pro Ser Tyr Gly
  67             180                   185                   190
  68 Phe Gln Tyr Ser Pro Ala Glu Arg Val Asp Phe Leu Leu Lys Ala Trp
  69         195                   200                   205
  70 Gly Ser Lys Lys Asp Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe
  71     210                   215                   220
  72 Asp Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile Tyr
  73 225                   230                   235                   240
  74 Gln Ala Cys Ser Leu Pro Gln Glu Ala Arg Thr Val Ile His Ser Leu
  75                   245                   250                   255
  76 Thr Glu Arg Leu Tyr Val Gly Gly Pro Met Thr Asn Ser Lys Gly Gln
  77         260                   265                   270
  78 Ser Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser
  79     275                   280                   285
  80 Met Gly Asn Thr Met Thr Cys Tyr Ile Lys Ala Leu Ala Ala Cys Lys
  81     290                   295                   300
  82 Ala Ala Gly Ile Val Asp Pro Val Met Leu Val Cys Gly Asp Asp Leu
  83 305                   310                   315                   320
  84 Val Val Ile Ser Glu Ser Gln Gly Asn Glu Glu Asp Glu Arg Asn Leu
  85                   325                   330                   335
  86 Arg Ala Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp
  87         340                   345                   350
  88 Leu Pro Arg Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser
  89     355                   360                   365
  90 Asn Val Ser Val Ala Leu Asp Ser Arg Gly Arg Arg Arg Tyr Phe Leu
  91     370                   375                   380
W--> 92 Thr Arg Asp Pro Thr Thr Pro (Xaa) Thr Arg Ala Ala Trp Glu Thr Val
  93 385                   390                   395                   400
  94 Arg His Ser Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Gln Tyr Ala
  95             405                   410                   415
  96 Pro Thr Ile Trp Val Arg Met Val Ile Met Thr His Phe Phe Ser Ile
  97         420                   425                   430
  98 Leu Leu Ala Gln Asp Thr Leu Asn Gln Asn Leu Asn Phe Glu Met Tyr
  99         435                   440                   445
 100 Gly Ala Val Tyr Ser Val Asn Pro Leu Asp Leu Pro Ala Ile Ile Glu
 101     450                   455                   460
 102 Arg Leu His Gly Leu Glu Ala Phe Ser Leu His Thr Tyr Ser Pro His
 103 465                   470                   475                   480
 104 Glu Leu Ser Arg Val Ala Ala Thr Leu Arg Lys Leu Gly Ala Pro Pro
 105     485                   490                   495
```

>? Xaa?

```
     106 Leu Arg Ala Trp Lys Ser Arg Ala Arg Ala Val Arg Ala Ser Leu Ile
     107             500             505                 510
     108 Ala Gln Gly Ala Arg Ala Ala Ile Cys Gly Arg Tyr Leu Phe Asn Trp
     109         515             520             525
     110 Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Leu Pro Glu Ala Ser Arg
     111         530             535                 540
     112 Leu Asp Leu Ser Gly Trp Phe Thr Val Gly Ala Gly Gly Gly Asp Ile
     113 545             550             555                 560
     114 Tyr His Ser Val Ser His Ala Arg Pro Arg Leu Leu Leu Leu Cys Leu
     115             565             570                 575
     116 Leu Leu Leu Ser Val Gly Val Gly Ile Phe Leu Leu Pro Asp Arg
     117         580             585                 590
     120 <210> SEQ ID NO: 2
     121 <211> LENGTH: 1776
     122 <212> TYPE: DNA
     123 <213> ORGANISM: Artificial Sequence
     125 <220> FEATURE:
     126 <223> OTHER INFORMATION: modified NS5B
W--> 128 <221> NAME/KEY: variation
     129 <222> LOCATION: (3)...(3)
     130 <223> OTHER INFORMATION: n = A or T
W--> 132 <221> variation
     133 <222> LOCATION: (9)...(9)
     134 <223> OTHER INFORMATION: n = C or A
W--> 136 <221> variation
     137 <222> LOCATION: (13)...(13)
     138 <223> OTHER INFORMATION: n = A or T
W--> 140 <221> variation
     141 <222> LOCATION: (15)...(15)
     142 <223> OTHER INFORMATION: n = A or C
W--> 144 <221> variation
     145 <222> LOCATION: (21)...(21)
     146 <223> OTHER INFORMATION: n - A or G
W--> 148 <221> variation
     149 <222> LOCATION: (24)...(24)
     150 <223> OTHER INFORMATION: n = C or G
W--> 152 <221> variation
     153 <222> LOCATION: (28)...(28)
     154 <223> OTHER INFORMATION: n = T or C
W--> 156 <221> modified_base
     157 <222> LOCATION: (30)...(30)
     158 <223> OTHER INFORMATION: n = G or C
W--> 160 <221> variation
     161 <222> LOCATION: (33)...(33)
     162 <223> OTHER INFORMATION: n = C or A
W--> 164 <221> variation
     165 <222> LOCATION: (71)...(71)
     166 <223> OTHER INFORMATION: n = A or G
W--> 168 <221> variation
```

```
       169 <222> LOCATION: (83)...(83)
       170 <223> OTHER INFORMATION: n = G or T
W--> 172 <221> variation
       173 <222> LOCATION: (1174)...(1174)
       174 <223> OTHER INFORMATION: n = A or C
W--> 176 <400> 2
W--> 177 tcnatgtcnt acncntggac nggngccntn atnacaccat gtgggcccga agaggagaag 60
W--> 178 ttaccgatca nccctctgag taattcgctc atncggttcc ataataaggt gtactccaca 120
       179 acctcgagga gtgcctctct gagggcaaag aaggtgactt ttgacagggt gcaggtgctg 180
       180 gacgcacact atgactcagt cttgcaggac gttaagcggg ccgcctctaa ggttagtgcg 240
       181 aggctcctca cggtagagga agcctgcgcg ctgaccccgc cccactccgc caaatcgcga 300
       182 tacggatttg gggcaaaaga ggtgcgcagc ttatctagga gggccgttaa ccacatccgg 360
       183 tccgtgtggg aggacctcct ggaagaccaa cataccccaa ttgacacaac tatcatggct 420
       184 aaaaatgagg tgttctgcat tgatccaact aaaggtggga aaagccagc tcgcctcatc 480
       185 gtataccccg acttggggt cagggtgtgc gaaaagatgg ccctctatga catcgcacaa 540
       186 aagcttccca aagcgataat ggggccatcc tatgggttcc aatactctcc cgcagaacgg 600
       187 gtcgatttcc tcctcaaagc ttggggaagt aagaaggacc caatggggtt ctcgtatgac 660
       188 acccgctgct ttgactcaac cgtcacggag agggacataa gaacagaaga atccatatat 720
       189 caggcttgtt ctctgcctca agaagccaga actgtcatac actcgctcac tgagagactt 780
       190 tacgtaggag ggcccatgac aaacagcaaa gggcaatcct gcggctacag gcgttgccgc 840
       191 gcaagcggtg ttttcaccac cagcatgggg aataccatga catgttacat caaagccctt 900
       192 gcagcgtgta aggctgcagg gatcgtggac cctgttatgt tggtgtgtgg agacgacctg 960
       193 gtcgtcatct cagagagcca aggtaacgag gaggacgagc gaaacctgag agctttcacg 1020
       194 gaggctatga ccaggtattc cgcccctccc ggtgaccttc ccagaccgga atatgacttg 1080
       195 gagcttataa catcctgctc ctcaaacgta tcggtagcgc tggactctcg gggtcgccgc 1140
W--> 196 cggtacttcc taaccagaga ccctaccact ccantcaccc gagctgcttg ggaaacagta 1200
       197 agacactccc ctgtcaattc ttggctgggc aacatcatcc agtacgcccc cacaatctgg 1260
       198 gtccggatgg tcataatgac tcacttcttc tccatactat tggcccagga cactctgaac 1320
       199 caaaatctca attttgagat gtacggggca gtatactcgg tcaatccatt agacctaccg 1380
       200 gccataattg aaaggctaca tgggcttgaa gccttttcac tgcacacata ctctccccac 1440
       201 gaactctcac gggtggcagc aactctcaga aaacttggag cgcctcccct tagagcgtgg 1500
       202 aagagtcggg cgcgtgccgt gagagcttca ctcatcgccc aaggagcgag ggcggccatt 1560
       203 tgtggccgct acctcttcaa ctgggcggtg aaaacaaagc tcaaactcac tccattgccc 1620
       204 gaggcgagcc gcctggattt atccgggtgg ttcaccgtgg gcgccggcgg gggcgacatt 1680
       205 tatcacagcg tgtcgcatgc ccgacccgc ctattactcc tttgcctact cctacttagc 1740
       206 gtaggagtag gcatcttttt actccccgat cgatga 1776
       208 <210> SEQ ID NO: 3
       209 <211> LENGTH: 1394
       210 <212> TYPE: PRT
       211 <213> ORGANISM: Artificial Sequence
       213 <220> FEATURE:
       214 <223> OTHER INFORMATION: modified NS3-5A
W--> 216 <221> NAME/KEY: VARIANT
       217 <222> LOCATION: (1215)...(1215)
       218 <223> OTHER INFORMATION: Xaa = asparagine or serine
W--> 220 <221> VARIANT
       221 <222> LOCATION: (904)...(904)
       222 <223> OTHER INFORMATION: Xaa = valine or alanine
W--> 224 <400> 3
```

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/577,893

DATE: 05/11/2006
TIME: 11:07:16

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

```
225 Met Ala Pro Ile Thr Ala Tyr Ser Gln Gln Thr Arg Gly Leu Leu Gly
226  1               5                  10                  15
227 Cys Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly
228             20                  25                  30
229 Glu Val Gln Val Val Ser Thr Ala Thr Gln Ser Phe Leu Ala Thr Cys
230         35                  40                  45
231 Val Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Ser Lys Thr
232     50                  55                  60
233 Leu Ala Gly Pro Lys Gly Pro Ile Thr Gln Met Tyr Thr Asn Val Asp
234 65                  70                  75                  80
235 Gln Asp Leu Val Gly Trp Gln Ala Pro Pro Gly Ala Arg Ser Leu Thr
236             85                  90                  95
237 Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala
238             100                 105                 110
239 Asp Val Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu
240         115                 120                 125
241 Ser Pro Arg Pro Val Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu
242     130                 135                 140
243 Leu Cys Pro Ser Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys
244 145                 150                 155                 160
245 Thr Arg Gly Val Ala Lys Ala Val Asp Phe Val Pro Val Glu Ser Met
246             165                 170                 175
247 Glu Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro
248             180                 185                 190
249 Ala Val Pro Gln Thr Phe Gln Val Ala His Leu His Ala Pro Thr Gly
250         195                 200                 205
251 Ser Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr
252     210                 215                 220
253 Lys Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly
254 225                 230                 235                 240
255 Ala Tyr Met Ser Lys Ala His Gly Ile Asp Pro Asn Ile Arg Thr Gly
256             245                 250                 255
257 Val Arg Thr Ile Thr Thr Gly Ala Pro Val Thr Tyr Ser Thr Tyr Gly
258             260                 265                 270
259 Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile
260         275                 280                 285
261 Ile Cys Asp Glu Cys His Ser Thr Asp Ser Thr Thr Ile Leu Gly Ile
262     290                 295                 300
263 Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val
264 305                 310                 315                 320
265 Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn
266             325                 330                 335
267 Ile Glu Glu Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr Gly
268             340                 345                 350
269 Lys Ala Ile Pro Ile Glu Ala Ile Arg Gly Gly Arg His Leu Ile Phe
270         355                 360                 365
271 Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Ser Gly
272     370                 375                 380
273 Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val
```

```
<210> 24
<211> 19
<212> DNA
<213> Artifial Sequence

<400> 24
gtctaccgtg agcgaggaa
```

If <213> Responses are Artificial or Unknown. Pls Explain the Source of genetic Material. See Item 11 on Error Summary Sheet.

```
<210> 27
<211> 783
<212> DNA
<213> modified NS4B
<400> 27
```

→ 22137 Responses can only be Artificial, Unknown or Genus Species. See Item 10 on Error Summary Sheet.

RAW SEQUENCE LISTING ERROR SUMMARY   DATE: 05/11/2006
PATENT APPLICATION: US/10/577,893   TIME: 11:07:17

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

Please Note:
Use of n and/or Xaa have been detected in the Sequence Listing. Please review the
Sequence Listing to ensure that a corresponding explanation is presented in the <220>
to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:1; Xaa Pos. 5,24,31,392
Seq#:2; N Pos. 3,9,12,15,21,24,28,30,33,71,93,1174
Seq#:3; Xaa Pos. 904,1215
Seq#:4; N Pos. 3644

Use of <220> Feature(NEW RULES):   OK
Sequence(s)__are missing the <220> Feature and associated headings.
Use of <220> to <223> is MANDATORY if <213> ORGANISM is "Artificial Sequence"
or"Unknown". Please explain source of genetic material in <220> to <223>
section (See "Federal Register," 6/01/98, Vol. 63, No. 104,pp.29631-32)
(Sec.1.823 of new Rules)

Seq#:1,2,3,4,24

VERIFICATION SUMMARY   DATE: 05/11/2006
PATENT APPLICATION: US/10/577,893   TIME: 11:07:17

Input Set : A:\21564Y SEQ 05 01 06.TXT
Output Set: N:\CRF4\05112006\J577893.raw

```
L:12 M:270 C: Current Application Number differs, Replaced Current Application No
L:12 M:271 C: Current Filing Date differs, Replaced Current Filing Date
L:27 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:31 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:35 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:39 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:43 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1
L:44 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:0
L:46 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:16
L:92 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:384
L:128 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:132 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:136 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:140 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:144 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:148 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:152 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:156 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:160 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:164 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:168 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:172 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:176 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2
L:177 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:0
L:178 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:60
L:196 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:1140
L:216 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:220 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:3
L:224 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:3
L:337 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:896
L:375 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:1200
L:411 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!
L:415 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:4
L:419 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:4
L:480 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:4 after pos.:3600
L:703 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:24
L:705 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ#:24, <213>
ORGANISM:Artificial Sequence
L:705 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:24, <213>
ORGANISM:Artificial Sequence
L:705 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:24,Line#:705
```